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L1 3289 S MCP OR (MONOCYTE (1W) CHEMOTACTIC (1W) PROTEIN)
L2 196 S L1 (P) ANTAGONIST?
L3 14 S L2 (P) TRUNCAT?
L4 630 S (MONOCYTE (1W) CHEMOTACTIC (1W) PROTEIN)
L5 102 S L4 AND ANTAGONIST
L6 4 S L5 AND TRUNCAT?

FILE 'CAPLUS, EMBASE, BIOSIS' ENTERED AT 14:31:26 ON 12 JUN 2001

L7 245 S L5
L8 7 S L6

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L3 ANSWER 4 OF 14 MEDLINE

AB Chemokines are important mediators in infection and inflammation. The **monocyte chemotactic proteins (MCPs)** form a subclass of structurally related C-C chemokines. **MCPs** select specific target cells due to binding to a distinct set of chemokine receptors. Recombinant and synthetic **MCP-1** variants have been shown to function as chemokine **antagonists**. In this study, posttranslationally modified immunoreactive **MCP-1** and **MCP-2** were isolated from mononuclear cells. Natural forms of **MCP-1** and **MCP-2** were biochemically identified by Edman degradation and mass spectrometry and functionally characterized in chemotaxis and Ca^{2+} -mobilization assays. Glycosylated **MCP-1** (12 and 13.5 kDa) was found to be two- to threefold less chemotactic for monocytes and THP-1 cells than nonglycosylated **MCP-1** (10 kDa). Natural, NH₂-terminally **truncated MCP-1**(5-76) and **MCP-1**(6-76) were practically devoid of bioactivity, whereas COOH-terminally processed **MCP-1**(1-69) fully retained its chemotactic and Ca^{2+} -inducing capacity. The capability of naturally modified **MCP-1** forms to desensitize the Ca^{2+} response induced by intact **MCP-1** in THP-1 cells correlated with their agonistic potency. In contrast, naturally modified **MCP-2**(6-76) was devoid of activity, but could completely block the chemotactic effect of intact **MCP-2** as well as that of **MCP-1**, **MCP-3**, and **RANTES**. Carboxyl-terminally processed **MCP-2**(1-74) did retain its chemotactic potency. Although comparable as a chemoattractant, natural intact **MCP-2** was found to be 10-fold less potent than **MCP-1** in inducing an intracellular Ca^{2+} increase. It can be concluded that under physiologic or pathologic conditions, posttranslational modification affects chemokine potency and that natural **MCP-2**(6-76) is a functional C-C chemokine inhibitor that might be useful as an inhibitor of inflammation.

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TITLE: Posttranslational modifications affect the activity of the human monocyte chemotactic proteins MCP-1 and MCP-2: identification of MCP-2(6-76) as a natural chemokine inhibitor.

AUTHOR: Proost P; Struyf S; Couvreur M; Lenaerts J P; Conings R; Menten P; Verhaert P; Wuyts A; Van Damme J

CORPORATE SOURCE: Rega Institute for Medical Research, Laboratory of Molecular Immunology, University of Leuven, Belgium.

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Complete crystal structure of monocyte chemotactic protein-2, a CC chemokine that ir with multiple receptors.

Biochemistry. 2000 Nov 21;39(46):14075-81.

PMID: 11087354 [PubMed - indexed for MEDLINE]

Related Resources

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Blood. 2000 Oct 15;96(8):2673-81.

PMID: 11023497 [PubMed - indexed for MEDLINE]

- ☐ 3: [Wuyts A, D'Haese A, Cremers V, Menten P, Lenaerts JP, De Loof A, Heremans H, Proost P, Van Damme J.](#) Relate

NH2- and COOH-terminal truncations of murine granulocyte chemotactic protein-2 au the in vitro and in vivo neutrophil chemotactic potency.

J Immunol. 1999 Dec 1;163(11):6155-63.

PMID: 10570306 [PubMed - indexed for MEDLINE]

- ☐ 4: [Proost P, Struyf S, Wuyts A, Menten P, De Meester I, Lambeir AM, Scharpe S, Schols D, De Clercq E, Van Damme J.](#) Relate

Isolation and identification of naturally modified C-C chemokines MCP-1, MCP-2 and RANTES: effects of posttranslational modifications on receptor usage, chemotactic an anti-HIV-1 activity.

Eur Cytokine Netw. 1998 Sep;9(3 Suppl):73-5. Review. No abstract available.

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Functional comparison of two human monocyte chemotactic protein-2 isoforms, role c amino-terminal pyroglutamic acid and processing by CD26/dipeptidyl peptidase IV.

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 Chemical synthesis, purification and folding of the human monocyte chemotactic prote MCP-2 and MCP-3 into biologically active chemokines.
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- ☐ 10: [Alam R, Forsythe P, Stafford S, Heinrich J, Bravo R, Proost P, Van Damme J.](#) Relate
 Monocyte chemotactic protein-2, monocyte chemotactic protein-3, and fibroblast-indu cytokine. Three new chemokines induce chemotaxis and activation of basophils.
 J Immunol. 1994 Oct 1;153(7):3155-9.
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